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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,004	05/10/2007	Thomas Koehler	PHDE040056US	8994

38107 7590 12/07/2009

PHILIPS INTELLECTUAL PROPERTY & STANDARDS
P. O. Box 3001
BRIARCLIFF MANOR, NY 10510

EXAMINER	
HOFFA, ANGELA MARIE	
ART UNIT	PAPER NUMBER
3768	
MAIL DATE	DELIVERY MODE
12/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,004	KOEHLER ET AL.	
	Examiner	Art Unit	
	Angela M. Hoffa	3768	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to communication filed on August 3, 2009.

Drawings

2. Applicant addresses the objection to the drawings made in the non-final Office Action in the response and indicates that replacement drawing sheets were submitted for Figures 2 and 4. However, these documents are not present in the file. Applicant's proposed amendment to the drawings is acceptable, but replacement drawing sheets are required. Therefore, the drawings remain objected to for the same reason as stated in the prior office action.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Amended Claim 11 recites the limitation of "a monitored blood flow rate of the patient". However, no mention of the monitoring of blood flow can be found within the disclosure. Applicant references monitoring the heart

beat rate as an indication of monitoring blood flow, but this feature is not synonymous with the measurement of blood flow and is therefore new matter.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,475,148 to *Jackson et al.*

Jackson et al discloses using a computer program to evaluate a heart beat rate of a heart of a patient, triggering a rupturing of a container comprising a drug on the basis of the evaluation of the heart beat rate (trigger device 26, Fig. 1, Col. 3 Lines 38-51), wherein the container is located in proximity to the part of the body resulting in a local application of the drug to the part of the body (Col. 3, Lines 29-37). Although *Jackson* does not disclose that this method is performed during a CT scan, the limitation of "during the CT scan" does not affect the steps of the method and is considered non-limiting functional language. However, this limitation will be treated as a positive limitation for the purposes of examination in the rejection below.

Regarding Claim 11, the limitation of "a monitored blood flow rate of the patient" is not present within Applicant's disclosure and is therefore not addressed here. However, an additional rejection is provided below and considers this limitation.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1-4, 7-9, 12-14, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,628,981 to *Baker et al* in view of the article titled "Noninvasive Visualization of Coronary Arteries Using Contrast-Enhanced Multidetector CT" to *Giesler et al* in further view of U.S. Patent No. 6,475,148 to *Jackson et al*.

Baker et al discloses imaging a patient during a CT scan (Fig. 1), monitoring the heart beat rate of the patient (EKG 46, Fig. 2; par. 0027), and correlating the imaging procedure with the heart beat rate of the patient (Sync Unit 48, Fig. 2; dynamic synchronization, par. 0027). *Baker et al* further discloses the importance of having a steady and predictable heartbeat during a CT scan in order to reduce motion artifacts (Col. 2, Lines 1-30).

However, *Baker et al* does not disclose using containers to deliver drugs to the patient or applying drugs to the patient to control his heart rate.

Giesler et al discloses a CT imaging procedure in which accuracy of cardiac imaging increases as the heart rate decreases. To decrease the heart rate, a drug is given to the patient (Conclusion section and Page 912, Col. 1, Lines 6-10).

Jackson et al discloses wherein drug-containing microbubbles are burst with ultrasonic waves in the heart (Col. 1, Lines 19-25, Col. 7, Line 31) in order to selectively deliver drugs for treatment (Col. 1, Line 66 – Col. 2, line 21).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to use an ultrasound microbubble technique to deliver drugs to slow a patient's heart during a CT scan ultrasound procedure in order to provide data with less motion artifact.

10. Claim 5 and 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,628,981 to *Baker et al* in view of the article titled "Noninvasive Visualization of Coronary Arteries Using Contrast-Enhanced Multidetector CT" to *Giesler et al* in further view of U.S. Patent No. 6,475,148 to *Jackson et al* as applied to Claim 1 above, in further view of U.S. Patent No. 5,542,935 to *Unger et al.*

Baker et al in view of *Giesler et al* in further view of *Jackson et al* does not expressly disclose using two sets of microbubbles with different resonant frequencies.

However, *Unger et al* discloses a microbubble drug delivery system that uses different sized microbubbles in order to change the resonant frequency of the application (Col. 30, Lines 58-63).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use multiple sets of microbubbles with different resonant properties, since it has been held that a mere duplication of the essential working parts of a device involves only routine skill in the art. St. Regis Paper Co. v. Bemis Co., 193 USPQ 8 and as taught by *Unger et al.*

11. Claim 6 and 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,628,981 to *Baker et al* in view of the article titled "Noninvasive Visualization of Coronary Arteries Using Contrast-Enhanced Multidetector CT" to *Giesler et al* in further view of U.S. Patent No. 6,475,148 to *Jackson et al* in further view of U.S. Patent No. 5,542,935 to *Unger et al* as applied to Claim 5 above, in further view of article "Control of Heart Rate" to *Kestin.*

Baker et al in view of *Giesler et al* in further view of *Jackson et al* in further view of *Unger et al* does not expressly disclose wherein application of drugs from the microbubble sets raises and lowers the patient's heart rate.

Baker et al discloses the importance of having a steady and predictable heartbeat during a CT scan in order to reduce motion artifacts (Col. 2, Lines 1-30), and *Giesler et al* discloses a CT imaging procedure in which accuracy of cardiac imaging

increases as the heart rate decreases. To decrease the heart rate, a drug is given to the patient (Conclusion section and Page 912, Col. 1, Lines 6-10).

Furthermore, *Kestin* discloses types of drugs that are used to regulate heart rate by increasing or decreasing properties that cause the heart to beat (adrenaline, anesthetic drugs, first page).

Since *Unger et al* and *Jackson et al* disclose many types of drugs that can be encapsulated into microbubbles and ultrasonically burst when they reach the target area, it would be obvious to use drugs to raise and lower the heart rate of a patient in order to obtain a steady and predictable heart rate for CT imaging as taught by *Baker et al* (Col. 2, Lines 1-30).

12. Claims 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,628,981 to *Baker et al* in view of the article titled "Noninvasive Visualization of Coronary Arteries Using Contrast-Enhanced Multidetector CT" to *Giesler et al* in further view of U.S. Patent No. 6,475,148 to *Jackson et al*.

Jackson et al discloses using a computer program to evaluate a heart beat rate of a heart of a patient, triggering a rupturing of a container comprising a drug on the basis of the evaluation of the heart beat rate (trigger device 26, Fig. 1, Col. 3 Lines 38-51), wherein the container is located in proximity to the part of the body resulting in a local application of the drug to the part of the body (Col. 3, Lines 29-37). *Jackson et al* further discloses wherein drug-containing microbubbles are burst with ultrasonic waves

in the heart (Col. 1, Lines 19-25, Col. 7, Line 31) in order to selectively deliver drugs for treatment (Col. 1, Line 66 – Col. 2, line 21).

Jackson does not disclose that this method is performed during a CT scan.

Baker et al discloses imaging a patient during a CT scan (Fig. 1), monitoring the heart beat rate of the patient (EKG 46, Fig. 2; par. 0027), and correlating the imaging procedure with the heart beat rate of the patient (Sync Unit 48, Fig. 2; dynamic synchronization, par. 0027). *Baker et al* further discloses the importance of having a steady and predictable heartbeat during a CT scan in order to reduce motion artifacts (Col. 2, Lines 1-30).

However, *Baker et al* does not disclose using containers to deliver drugs to the patient or applying drugs to the patient to control his heart rate.

Giesler et al discloses a CT imaging procedure in which accuracy of cardiac imaging increases as the heart rate decreases. To decrease the heart rate, a drug is given to the patient (Conclusion section and Page 912, Col. 1, Lines 6-10).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to use an ultrasound microbubble technique to deliver drugs to slow a patient's heart during a CT scan ultrasound procedure in order to provide data with less motion artifact.

13. Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,475,148 to *Jackson et al.*

Jackson et al discloses using a computer program to evaluate a heart beat rate of a heart of a patient, triggering a rupturing of a container comprising a drug on the basis of the evaluation of the heart beat rate (trigger device 26, Fig. 1, Col. 3 Lines 38-51), wherein the container is located in proximity to the part of the body resulting in a local application of the drug to the part of the body (Col. 3, Lines 29-37).

However, *Jackson* does not disclose wherein a blood flow rate of the patient is monitored.

However, it would have been obvious to one of ordinary skill in the art at the time of invention that correlating the drug delivery with a heart beat rate performs the same intended use of correlating the drug delivery with a blood flow rate, in order to delivery the drug at the right point in time at the intended area. Therefore, monitoring the blood flow and monitoring the heart beat rate are considered synonymous for performing the steps of the method.

Response to Arguments

14. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the Baker reference does not disclose the limitation of "monitoring a heart beat rate of the patient during the CT scan". Although Applicant has correctly interpreted the Baker reference, the limitation seems to have been overlooked in its disclosure within Par. 0027 of Baker, "Although the activation of the x-ray beam can be dynamically synchronized to each cardiac cycle which occurs *during the scan*...". As is common in the art, the Baker reference discloses a cardiac gating technique in order to

align a desired phase of the cardiac cycle to the acquisition of the image (specifically a resting phase, par. 0026). It is the other imaging parameters such as slice thickness and gantry speed that are not dynamically changed during imaging but are based off of a predicted heart rate obtained prior to imaging. Applicant further argues regarding the Baker reference, that monitoring a cardiac phase is not the same as monitoring a heart beat rate. However, in measuring repeating cardiac phases and triggering image acquisition based on the repeating cardiac phase, a heart beat rate is inherently measured and images are acquired at the heart beat rate (i.e. the rate of occurrence of the specific cardiac phase).

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela M. Hoffa whose telephone number is 571-270-7408. The examiner can normally be reached on Monday - Friday, 9:00 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/A. M. H./
Examiner, Art Unit 3768

/Long V Le/
Supervisory Patent Examiner, Art Unit 3768